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Original Research

Risk factors for current wheeze among school children (6–7 and 13–14 years old) in Khuzestan, Iran

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ABSTRACT

Objectives: In recent years, there has been a clear trend of increasing allergic diseases especially in children, and developing countries are no exception. Thepresentstudy sought to determine the risk factors associated with wheezing among school children aged 6–7 and 13–14 years living in Khuzestan Province, Iran.
Study design: Cross-sectional.
Methods: Data for this cross-sectional study is the history of wheeze in the last 12 months. The participants included 6-7- and 13-14-year-old girls and boys studying in urban schools in Khuzestan Province in 2019. We collected the data using the multi stage sampling technique as suggested in the International Study of Asthma and Allergies in Childhood (ISAAC). The research reviewed the literature and consulted experts to collect the risk factors for demographic and clinical information, environmental exposure and lifestyle.
Results: Eight thousand questionnaires were handed out to both age groups, of which 7344 were completed. Two hundred ninety-nine (4.1 %) of the participants had current wheeze. Three-point four percent (124 individuals) in the 6–7 year age group and 4.8 % in the 13–14-year-old age group had current wheezing. The results of the logistic regression model suggest that the most significant risk factors associated with the chance of developing current wheeze in the both age groups are: being male (OR: 1.46, 95 % CI: 1.12–1.88), being from employed mother families (OR: 1.50, 95 %, CI:1.05–2.08), property ownership (OR:1.36, 95 %, CI:1.04–1.79) bugs in the property (OR: 1.29, 95 %, CI:0.99–1.70) mold in the property (OR: 1.75, 95 %, CI:1.12–2.76), pet(s) in the student's bedroom (OR: 1.75, 95 %, CI: 0.97–3.14), a family history of asthma and allergic diseases (OR: 2.20, 95 %, CI: 1.69–2.87), tobacco smoke exposures in the property (OR: 1.43, 95 %, CI:1.04–1.96), having allergic rhinitis (OR: 7.86, 95 % CI: 5.89–10.50) and eczema (OR: 3.85, 95 % CI: 2.10–7.08).
Conclusions: Families are suggested to adopt strategies to reduce exposure to outdoor air pollutants and contain indoor allergens. More studies are necessary to further explore the effects of modifying and changing these risk factors.

1. Introduction

Allergic disorders are closely linked; an allergic disorder might increase the likelihood of developing another one [1]. Allergic disorders are estimated to affect 40% of the world's population. According to the reports, asthma, allergic rhinitis and eczema are more prevalent than other allergies [2]. Allergic rhinitis is an inflammatory disease, affecting the mucous membranes of the nose. The clinical symptoms of allergic rhinitis are rhinorrhea, sneezing, itchy nose, eyes, conjunctiva, ears and throat [3,4]. Atopic eczema is the most common inflammatory disease of the skin in childhood [5]. Atopic eczema is the first stage in allergic diseases, often characterized by a chronic itchy skin rash [6]. Compared

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to other inflammatory disorders, asthma is more prevalent in children, making it a major health and even economic challenge. Symptoms include wheezing, shortness of breath, chest tightness, and frequent coughing [7]. Simultaneous occurrence of asthma, allergic rhinitis and eczema causes the symptoms to appear more severely and have an adverse effect on quality of life [8].

In recent decades, the world has seen a significant increase in allergic diseases, especially in children, and developing countries are no exception [9]. According to studies conducted in the Middle East, the prevalence of allergic diseases in the region is usually lower than in developed countries, however, it is on the rise [10,11]. The overall prevalence of asthma among children in the Middle East is estimated to be between 10 and 30 % with the highest incidence in Saudi Arabia (23 %). The highest prevalence of allergic rhinitis was reported in Morocco (37.8 %) and eczema in Qatar (23 %) [10]. In 2011, the prevalence of asthma was generally reported to be 3.9 % among Iranian children. It is higher in boys than girls (4.3 % and 3.2 %, respectively) [12]. The prevalence of the disease in Iran is different for each province. Reports obtained with the ISAAC questionnaire indicate the highest prevalence of asthma in Tehran Province and the lowest in Kermanshah Province [13]. According to a recent demographic survey in Iran, the maximum prevalence of asthma in Iranian children aged 6 to 7 was 15 %, and it was higher in adolescents aged 13 to 14 in nine provinces. The highest prevalence was reported for the south, northeast and some central provinces in both age groups [14]. This trend in the prevalence of asthma suggests that environmental factors may influence the onset and progression of these diseases. Genetics and environment are two important factors in developing allergic diseases. Environmental factors play a major role in developing asthma and allergic diseases. Internal and external environmental risk factors include: diet, lifestyle, stress, use of antibiotics, family size, parental smoking, contact with pets, attending kindergarten, respiratory tract diseases, intestinal worm infections, eating habits at the beginning of life (which affects the immune system) [15,16]. Climate change, global warming, and air pollution, especially in developed countries contribute to the rapid spread of allergic disorders [17,18]. The reason for the increase in prevalence may vary for each region. Epidemiological studies around the world report different risk factors that contribute to developing asthma. Despite the myriad risk factors that affect allergic diseases, information about environmental exposure, lifestyle and other factors associated with increased prevalence of the allergic diseases in Khuzestan Province is very limited. Therefore, this is the first study to investigate the risk factors associated with current wheezing among students aged 6–7 and 13–14 in Khuzestan Province, Iran.

2. Methods

This study was undertaken in Khuzestan Province in southwestern Iran, located at 31.33 ° N and 48.69 °E. Khuzestan Province is the heart of oil and gas production in Iran. It covers an area of 64,055 square kilometers and, with a 4711000 population, it is considered as the fifth most populous province in Iran.

This descriptive-analytical cross-sectional study was conducted in 2019 on 3681 students aged 6–7 years and 3663 students of 13–14 years, girls and boys, in urban schools of Khuzestan Province via the multistage sampling technique. We used the International Study of Asthma and Allergies in Childhood (ISAAC) scale to collect data on the history of current wheeze, allergic rhinitis and eczema in the past 12 months.

Our checklist includes: demographic variables, environmental factors (internal/external) and as well as a history of allergic rhinitis during the last 12 months and having eczema (Table 1- Supplementary).

2.1. Sample size

A study by Ghaffari et al. (2012) in Sari, Iran found the prevalence of pediatric asthma as12 %, the incidence of rhinitis as 17 %, and the prevalence of eczema as 6 % [19]. For more accurate results, we calculated the sample size based on the lowest prevalence rate (6 %). Given that the cluster effect is 1.5, the final sample size reached 4000 individuals in all grades of the elementary school children (6–7year old children) and the first graders (13–14 years of age). The sample size formula is presented below.

2.2. Sampling

First, we used stratified sampling to categorize the schools in Khuzestan into five geographical areas: North, south, east, west and the center. Then, the researchers used random cluster sampling to select urban schools in each area. Through arrangements with the Education & Training Department of Khuzestan Province, Iran, we compiled a list of primary and secondary schools in Khuzestan Province along with their location and population. The number of clusters required for each geographical area, in proportion to their population ratio, was selected from the total population of schools in the province. In the next step, cluster sampling of primary schools was performed within each geographical area. Finally, we selected 100 clusters (schools) each including 40 students from all primary schools in Khuzestan Province through systematic sampling. After selecting clusters (schools) in each elementary school, we examined the first elementary student (age group 6–7 years) by systematic sampling. The purpose was to select 40 students. We did the cluster sampling of middle schools in each urban geographical area in the same manner. The research examined the first middle school students within each middle school (13–14 years old age group) by systematic sampling. Finally, 4000 samples were included from each elementary and middle school. In the 6–7-yearage group children, the questionnaires were completed by the parents, while in the 13–14 year age group, children filled the questionnaire.

The researchers obtained the required permits to conduct research and made arrangements with the authorities. These included:

1 Obtaining the approval for the research proposal
2 Obtaining the ethics code from the Ethics Committee of Ahvaz University of Medical Sciences
3 Obtaining permission from the Education & Training Department of Khuzestan Province to enter primary and secondary schools

Informed written consent was obtained from the respondents (for the 6–7 year old group, the research obtained parental consent). They also ensured that their information was kept confidential.

2.3. Analysis

The study used descriptive statistics including frequency, median and first quarter and third quarter. To investigate the relationship between the dependent variable and predictor variables, the research used the univariate logistic regression model. Variables whose P-value was less than 0.2 were selected to enter the multiple logistic regression analysis models. To determine the most influential factors associated with current wheeze, we applied a backward stepwise logistic regression modeling. The odds ratio (OR) and 95 % confidence interval (CI) were reported. The data was analyzed with Software R3.5.1. P-values less than 0.05 were considered significant.

3. Results

Eight thousand questionnaires were distributed and 7344 were completed. The response rate was 92 %. Among 7344 students, 299 (4.1 %) had current wheeze.

The results of the univariate logistic regression model suggest that the chances of current wheeze in people with allergic rhinitis and eczema were 11.8 (CI: 95 %, 1–15.41, $P < 0.001$) and 8.9 (CI: 95 %, 5.42–14.76, $p < 0.001$), respectively, higher than individuals who did

not have allergic rhinitis and eczema. The likelihood of current wheeze in students who had a pet in their bedroom (OR: 3.45, 95 %, CI: 2.05–5.81, $p < 0.001$) and a family history of asthma and allergic diseases (OR: 3.22, 95 %, CI: 2.54–4.10, $p < 0.001$) was significantly higher. Other risk factors related to current wheeze are presented in Tables 1 and 2.

Based on the results of the multiple logistic regression model, the strongest possible risk factors for current wheeze in students are as follows: being male, being from employed mother families, home ownership, bugs and mold at home, pet in the student's bedroom, green space within 200 m of residence, a family history of asthma and allergic diseases, smoker (s)in the household and having allergic rhinitis and eczema (Table 3).

Three-point four percent (124 individuals)of the 6–7 year old age groupand4.8 % (175 individuals) of the 13–14 year old age group had current wheeze. Current wheeze was observed in 3.1 % (n = 105) of the school girls and 4.9 % (n = 194) in school boys.

4. Discussion

Due to the increasing prevalence and burden of allergic diseases, it is highly important to take measures to prevent, diagnose and treat the disease in time [20]. This research studied some factors that may play a significant role in the morbidity of current wheeze in Khuzestan Province.

The results showed that these factors increase the chances of developing current wheeze: gender (being a boy), age (age group 13–14 years), low birth weight, not being breastfed, being from an employed motherfamily, a family history of asthma and allergies, smoker in the household, residing in a villa, house ownership compared to being a tenant, having a garden at home, having damp, mold and bugs in the house, having a pet in the home or child's bedroom, having allergic rhinitis and eczema, as well as increased lifespan of the property. The final logistic regression model showed that the strongest possible risk factors associated with current wheeze were being male, being from an employed motherfamily, owning the property, bugs and mold at home, pet in student's bedroom, green space near the property, a family history of asthma and allergic diseases, a smoker at home and having allergic rhinitis and eczema.

This study indicates that gender is an important determinant of the prevalence of current wheeze in Khuzestan Province. In this regard, our findings are in line with the results of a meta-analysis conducted in the population of Iranian children on the higher prevalence of asthma symptoms among boys than girls (4.3 % vs. 3.2 %) [12]. In addition, in another study in western Iran, the symptoms of allergic rhinitis, including sneezing and runny nose, were more common in boys than girls in both groups of 6-7-yearold and 13-14-yearolds children [21]. The anatomical condition and lower ratio of airway diameters to lung volume in boys explain the higher prevalence of asthma among them [22]. Some studies suggest that genetically responsive to allergens and the development of allergic sensitivity are more common in boys than in girls [23,24].

In line with our results on the important role of age, a 2016 study in India estimated the prevalence of allergic rhinitis, allergic rhinoconjunctivitis and eczema in 13- to 14-year-olds at 24.4, 10.9 and 3.7 %, respectively. Meanwhile, these three complications in children 6 7-year-olds had a lower prevalence (11.3 %, 3.9 % and 2.8 %, respectively) [25]. Higher prevalence of asthma and allergic diseases in adolescence than childhood has been reported in different regions in Iran [14,26–28]. äBäcklund's study in Sweden explains why the prevalence of asthma increases from 7 to 8 years old to 11–12 years old. It seems that wheezing in children is not considered as asthma, while it is diagnosed as asthma in older children [29].

The presence of concomitant allergic diseases, including allergic rhinitis and eczema, has been shown to be an important risk factor for asthma in children in other studies [30–33]. VonKobyletzki and

Table 1
Demographic and clinical risk factors for current wheeze (Univariate logistic regression).

Characteristics	Without current wheeze	With current wheeze	Odds ratio	95 % CI	P-value
Gender					
Girl	3250 (96.9)	105 (3.1)	Ref	–	<0.001*
Boy	3795 (95.1)	194 (4.9)	1.58	1.24–2.02	
Age group					
6–7	3557 (96.6)	124 (3.4)	Ref	–	0.002*
13–14	3488 (95.2)	175 (4.8)	1.44	1.14–1.82	
Birth season					
Spring	1646 (94.8)	91(5.2)	Ref	–	–
Summer	1827 (95.8)	80(4.2)	0.79	0.58–1.08	0.137
Fall	1495 (95.9)	64(4.1)	0.77	0.56–1.07	0.126
Winter	1320 (95.9)	57(4.1)	0.78	0.56–1.10	0.153
Type of birth					
Term	6840 (95.9)	291 (4.1)	Ref	–	0.143
Premature	92(92.9)	7(7.1)	1.79	0.82–3.89	
Birth weight					
Normal	6702 (96.0)	281 (4.0)	Ref	–	0.017*
Low birth weight	218 (92.8)	17(7.2)	1.86	1.12–3.09	
Breast feeding					
Yes	5880 (96.2)	232 (3.8)	Ref	–	0.001*
No	1052 (94.1)	66(5.9)	1.59	1.20–2.11	
Father'seducation[a]					
Illiterate/Low	1974 (96.0)	119 (4.6)	0.95	0.70–1.29	0.745
Moderate	2447 (95.4)	88(4.2)	1.10	0.83–1.46	0.511
High	1989 (95.8)	290 (4.3)	Ref	–	–
Mother's education[a]					
Illiterate/Low	2175 (95.8)	95(4.2)	0.94	0.68–1.29	0.691
Moderate	2785 (95.6)	128 (4.4)	0.99	0.73–1.34	0.926
High	1394 (95.5)	65(4.5)	Ref	–	–
Father's job					
Unemployed	199 (95.7)	9(4.3)	Ref	–	0.990
Employed	6151 (95.7)	277 (4.3)	1.00	0.50–1.96	
Mother's job					
Housekeeper	6126 (96.1)	246 (3.9)	Ref	–	0.003*
Employed	751 (93.9)	49(6.1)	1.62	1.18–2.23	
Family size					
≤ 3	1058 (95.5)	50(4.5)	Ref	–	0.776
>3	5402 (95.7)	244 (4.3)	0.96	0.70–1.30	
Family history of asthma					
No	5470 (96.9)	174 (3.1)	Ref	–	<0.001*
Yes	1180 (90.7)	121 (9.3)	3.22	2.54–4.10	
Smoker in the household					

(continued on next page)

Table 1 (*continued*)

Characteristics	Without current wheeze	With current wheeze	Odds ratio	95 % CI	P-value
No	5790 (96.2)	230 (3.8)	Ref	–	<0.001*
Yes	866 (92.8)	67(7.2)	1.95	1.47–2.58	
Rhinitis in the last 12 months					
No	6761 (97.1)	200 (2.9)	Ref	–	<0.001*
Yes	284 (74.2)	99 (25.8)	11.78	9.01–15.41	
Eczema ever					
No	6983 (96.2)	277 (3.8)	Ref	–	<0.001*
Yes	62(73.8)	22 (26.2)	8.94	5.42–14.76	

Values presented as No. (%), unless otherwise stated.

*P Values is significant.

[a] Low educational level (primary school & middle school), moderate educational level (high school and associated degree), and high educational level (bachelor, master and doctorate degree).

colleagues in their study in Sweden reported that children with a history of eczema were three times more likely to develop asthma than children without eczema [34]. According to the results of other studies, in patients with allergic rhinitis, the prevalence of asthma is reported to be between 55 % and 79 %, with the severity of allergic rhinitis being directly related to the severity of asthma [35]. Similarly, a study by Deliu et al. showed that children with allergic rhinitis experienced 2.89 times more recurrent attacks of wheezing and 3.44 times more severe attacks [36].

In some studies, the history of asthma and family history of allergies have been reported as the most important factors influencing the occurrence of asthma in children aged 3–11 years [37]. Consistent with the results of the present study, Sheikh et al. in their study in Ohio, USA, reported a 71.4 % family history of asthma in people with asthma aged 1–20 years, which was higher in mothers (28.5 %) than fathers (18.7 %) [38]. The association between childhood asthma and the family history of distant relatives, including grandparents, has also been observed [38–40], and the more people with the disease in the family, the more likely children are to get asthma [39]. Children with a family history of asthma have also been shown to be at greater risk for environmental factors [38].

Consistent with the results of this study, literature confirms smoking cigarettes as an important risk factor for asthma and its symptoms. For

Table 2
Environmental risk factors (internal/external)for current wheeze (Univariate logistic regression).

Characteristics	Without current wheeze	With current wheeze	Odds ratio	95 % CI	P-value
Accommodation type					
Apartment	2438(96.6)	85(3.4)	Ref	–	0.006*
House	4159(95.2)	85(4.8)	1.43	1.11–1.86	
Property ownership					
Tenant	2373(96.3)	90(3.7)	Ref	–	0.040*
Landlord	4128(95.3)	204(4.7)	1.30	1.01–1.68	
Garden in property					
No	5125(96.3)	196(3.7)	Ref	–	0.004*
Yes	1874(94.8)	103(5.2)	1.44	1.13–1.84	
Green space					
No	2682(96.2)	105(3.8)	Ref	–	0.079
Yes	3924(95.4)	191(4.6)	1.24	0.98–1.59	
Largest path within 100 m of home					
Auxiliary road	2126(95.8)	93(4.2)	Ref	–	0.774
Main street	4473(95.7)	203(4.3)	1.04	0.81–1.33	
Opening the windows more than 30 min in a day					
No	2197(95.9)	93(4.1)		–	0.526
Yes	4422(95.6)	203(4.4)	1.08	0.84–1.39	
Humid rooms					
No	4735(96.2)	185(3.8)	Ref	–	0.001*
Yes	1864(94.4)	111(5.6)	1.52	1.20–1.94	
Mold in property					
No	6323(96.0)	266(4.0)	Ref	–	<0.001*
Yes	280(90.3)	30(9.7)	2.55	1.71–3.78	
Bugs in property					
No	4897(96.4)	184(3.6)		–	<0.001*
Yes	1711(93.9)	112(6.1)	1.74	1.37–2.22	
Pet in property					
No	5993(96.2)	235(3.8)	Ref	–	0.001*
Yes	1000(94.0)	64(6.0)	1.63	1.23–2.17	
Pet in bedroom					
No	6865(96.1)	282(3.9)	Ref	–	<0.001*
Yes	120(87.6)	17(12.4)	3.45	2.05–5.81	
Cleaning utensil					
Electric	6756(96.0)	281(4.0)	Ref	–	0.019*
Sweeper	240(93.0)	18(7.0)	1.80	1.10–2.95	
Rug in room					
No	332(95.7)	15(4.3)	Ref	–	0.975
Yes	6273(95.7)	281(4.3)	0.99	0.58–1.69	
	Median (Q1-Q3)	**Median (Q1-Q3)**			
Residential area	100.0(85.0–137.0)	100.0(85.0–150.0)	1.00	1.00–1.00	0.591
Duration of stay in the current property	5.0(2.0–10.0)	6.0(2.0–10.0)	1.02	1.00–1.03	0.073
Building age	10.0(5.0–17.0)	12.0(7.0–20.0)	1.01	1.00–1.02	0.008*

Values presented as No. (%), unless otherwise stated.

*P Values is significant.

Table 3
The important risk factors for current wheeze (multiple logistic regression).

Characteristics	Odds ratio	95 % CI	P-value
Gender			
Girl	Ref.	–	0.005*
Boy	1.46	1.12–1.88	
Mother's job			
Housekeeper	Ref.	–	0.024*
Employed	1.50	1.05–2.08	
Property ownership			
Tenant	Ref.	–	0.026*
Landlord	1.36	1.04–1.79	
Bugs in property			
No	Ref.	–	0.059
Yes	1.29	0.99–1.70	
Mold			
No	Ref.	–	0.015*
Yes	1.75	1.12–2.76	
Pet in bedroom			
No	Ref.	–	0.062
Yes	1.75	0.97–3.14	
Green space			
No	Ref.	–	0.111
Yes	1.24	0.95–1.60	
A family history of asthma			
No	Ref.	–	<0.001*
Yes	2.20	1.69–2.87	
Smoker in the household			
No	Ref.	–	0.027*
Yes	1.43	1.04–1.96	
Rhinitis in the last 12 months			
No	Ref.	–	<0.001*
Yes	7.86	5.89–10.50	
Eczema ever			
No	Ref.	–	<0.001*
Yes	3.85	2.10–7.08	

*P Values is significant.

example, Wang et al. showed that children with asthma who are exposed to secondhand smoke are more likely to show current wheeze and get admitted to emergency wards compared to children with asthma who are not exposed to smoking; They are even twice as likely to be hospitalized [41]. In the study by Singh in India [25] and Fazlollahi in Iran [14], smoking cigarettes is reported as the most significant risk factor associated with allergic disease in both age groups 6–7 and 13-14-years old children. According to a study in Manitoba, parents of children with asthma are less likely to change their smoking behavior (quit smoking or smoke outside the property) [42].

In line with the results of the present study, other studies support a higher risk of asthma morbidity and related symptoms in children who are in contact with pets, including dogs, cats, and birds [20,43,44]. In a recent study in Kuwait, the risk of current asthma and allergic rhinitis was 287 % and 84 % higher in children aged 11–14 years exposed to poultry [45]. Given that the number of families keeping pets in Khuzestan Province is increasing, this can play a role in the prevalence of allergic diseases.

Bugs in the property is another risk factor. At least two randomized controlled clinical trials in children with asthma in the United States have shown that asthma symptoms improve by 50–90 % with less exposure to bugs [46,47]. Other risk factors for the indoor environment are damp and mold. Two studies in China confirmed a positive association between damp and mold in a child's bedroom and an increased risk of symptoms of allergic diseases, including asthma [16,48]. In the United Kingdom, damp and mold doubled the risk of developing asthma [49]. Older properties are more prone to damp and mold. As a result, children are more likely to develop asthma than those living in new properties.

Reports from Malaysia, Australia, and the United Kingdom, suggest that students who are underweight at birth are more likely to have wheezing than normal weight students [50–52]. Another risk factor was using ahand sweeper for cleaning the house. Dust removal activities from carpets and furniture by sweepers disperse dust, while electric cleaners help reduce the concentration of sediment particles [53]. Having a garden at home and contact with allergenic shrubs, was confirmed as a risk factor. Some flowers and trees that release allergenic pollen or spores aggravate allergic diseases and cause airway obstruction [54–56]. Probably one of the factors that makes living in a villa house a risk factor is a garden and higher exposure to other environmental factors.

4.1. Strengths and limitations

This study was the first to determine the risk factors of current wheeze in children and adolescents in Khuzestan Province. The vastness of the study area, which includes different cities of Khuzestan Province with different urban, geographical and environmental characteristics, was another strength of this study. However, this study has limitations too. Firstly, this study explains the association between exposure to risk factors for demographic, clinical, environmental, and lifestyle factors with current wheeze, however, it is not possible to prove that exposure to these risk factors is the main cause of current wheeze in children and adolescents. Second, this study used self-reported data based on the ISSAC questionnaire, so some bias is probable.

5. Conclusion

The strongest possible risk factors associated with current wheeze were male gender, employed mother, owning status of the residence, beetles and mold at home, pet in student bedroom, green space near the residence, family history of asthma and allergic diseases, a smoker at home and having allergic rhinitis and eczema. Adopting strategies by households to reduce exposure to open space pollutants as well as allergens in the home seems necessary. Moreover, more studies need to focus on the impacts of modifying and changing these risk factors.

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Declaration of competing interest

The authors declare that they have no competing interests.

Ethics approval

Ethics License of the present study was acquired from the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (Code of ethics: IR. AJUMS.REC.1395.358).

Consent to participate

The study obtained parental written consent on voluntary participation was received. Parents were assured that their information would remain confidential.

Consent for publication

Not applicable.

Availability of data and material

Data sharing: Participant level data could be obtained from the corresponding author.

Code availability

Not applicable.

Authors' contributions

EI, MD and HR conceived and designed the project. MD and ES acquired the data. MD and FM analyzed and interpreted the data. NK and MHS wrote the paper. All authors approved the final text.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhip.2021.100172.

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